DEPARTMENT OF HEALTH SERVICES
GENETIC DISEASE BRANCH
2151 BERKELEY WAY, ANNEX 4
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Newborn Screening Program
Tandem Mass Spectrometry (MS/MS) Research Project
Fact Sheet For Pediatric Care Providers

Background Information

"The introduction of Tandem Mass Spectrometry (MS/MS) in the 1990's for population-based newborn screening has enabled health-care providers to detect an increased number of metabolic disorders in a single process by using dried blood spot specimens routinely collected for newborn screening. "[1] MS/MS allows for screening of multiple metabolic disorders using a single analytical run. With this technology there is the potential to test for a wide array of metabolic disorders, including amino acid disorders, organic acidemias, and fatty acid oxidation disorders *(see list of disorders)*. Because the technology can detect these disorders (approximately 30 total) within 1 to 2 minutes, the system can handle the large numbers of specimens required in newborn screening. For some of the disorders identifiable via MS/MS, such as medium chain acyl-CoA dehydrogenase deficiency (MCAD), early detection and treatment can result in substantial improvements in health outcomes (i.e., prevention of mortality and improvement of the quality of life). Several states have already expanded, or are in the process of expanding, their newborn screening program to add these disorders.

The California Newborn Screening Program (NBSP) in the Department of Health Services, Genetic Disease Branch has been in existence since 1980 and currently tests for PKU, galactosemia, primary congenital hypothyroidism, sickle cell disease and other hemoglobinopathies. On September 28, 2000, Governor Gray Davis signed into law Assembly Bill 2427 (Kuehl) which provides for updating and expanding the newborn screening program in California. The law took effect on January 1, 2001. AB 2427 requires the Department of Health Services to establish a new and broader testing program, including development and evaluation of expanded genetic disease testing utilizing MS/MS. In response, the Department is in the process of initiating a pilot (research) project, which is scheduled to start on or shortly after January 7, 2002.

Overview of the NBS MS/MS Research Project

This study is being conducted in part to determine which of the disorders identifiable via MS/MS meet the criteria for inclusion in California's mandatory Newborn Screening Program, i.e., which of the unusual results have clinical significance and/or warrant reporting. Almost all "interesting" or "unusual" results will be reported out to the primary care provider and referred to the California Children's Services (CCS)-approved Metabolic Center for evaluation. Treatment and outcome data will be collected on all newborns referred to California Children's

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[1] Centers for Disease Control and Prevention. Using Tandem Mass Spectrometry for Metabolic Disease Screening Among Newborns: A Report of the Workgroup—Georgia, 2000. *MMWR Morb Mortal Wkly Rep., Recommendations and Reports* April 13, 2001:50:1

Services (CCS) Metabolic Centers for follow-up. The estimated duration of the supplemental testing is 12-18 months. Participation in the study will be voluntary and informed consent will be obtained for both the testing of specimens and for release of medical information for newborns referred to metabolic centers for follow-up. There will be no additional fee charged for participation in the supplemental screening. Based upon 515,000 annual California births and an acceptance rate similar to other states that have offered MS/MS supplemental screening, we are projecting about 400,000 newborns being screened via MS/MS during the pilot period. We anticipate detecting 40-60 newborns with clinically significant metabolic disorders currently that are not detected through the mandatory newborn screening program.

Role of Pediatric Care Providers

Pediatric Care Providers should be knowledgeable about the supplemental screening program, be available to answer questions, and provide additional information to parents and hospital staff. They should collaborate with the MS/MS Follow-up Coordinators to refer patients with unusual screening results to a CCS-approved metabolic center specialist. However, pediatric care providers should report and follow up on any unusual signs and symptoms observed while a child is in their care even if the newborn screen is normal***. All diagnosed cases of metabolic disorders identifiable via MS/MS in newborn period (see list of disorders) should be reported to the Department of Health Services Genetic Disease Branch (GDB) whether disorders were detected via screening or not.***

Reporting of Screening Results

Hospitals and the pediatric care providers listed on the Newborn Screening Test Request Form (Specimen Collection Form) receive a written report on the mandatory screening program. However, during the research project, hospitals will not receive results on the supplemental screening. Only "unusual results" of the supplemental screening will be reported, and the report will go to the pediatric care provider listed on the Newborn Screening Test Request Form. To expedite the process of follow-up of newborn screening results for both the mandatory and supplemental programs, hospital staff completing the Newborn Screening Test Request Form need to enter the correct name and address of the pediatric care provider who will be following each newborn after hospital discharge (the newborn's "medical home"). Pediatric care providers should make sure that the hospital has the correct information.

Follow-up for Unusual Results

For newborns with unusual results, the pediatric care provider will be contacted via telephone by the MS/MS Follow-up Coordinator and the newborn will subsequently be referred by the MS/MS Follow-up Coordinator to one of the CCS-approved Metabolic Centers for diagnosis and initiation of treatment. The Metabolic Centers will make the arrangements for confirmatory testing and develop the diagnostic and treatment plan, which will be conveyed to the primary care provider and the Newborn Screening Program. Based upon the experience of the research project and input from the metabolic specialists, follow-up guidelines for these conditions will be developed.

Key Points to Emphasize with Parents

- No additional blood will be taken from the newborn.
- Knowledge gained from this project will be used to expand the program in the future to improve screening for newborns and families.
- All disorders may not be detectable, i.e., there will probably be disorders that are missed.
- There could be some benefit to families who participate e.g., early detection and treatment for newborns with one of the disorders.
- Negative supplemental screening results will not be reported to the pediatrician.
- If a specimen is inadequate, the supplemental testing will not be run and parents will not be offered repeat supplemental testing through the program.
- If there is a family history of metabolic disorders or if the family has concerns, they should be offered information on obtaining supplemental testing outside of, or ***in addition to***, ***the research study***. Optional supplemental screening is offered for a fee by Baylor University Medical Center (Dallas, Texas http://www.baylordallas.edu), or NeoGen Screening Inc. (Bridgeville, Pennsylvania http://www.neogenscreening.com).
- There is no additional cost for the voluntary supplemental screening test.
- Private Insurance, Medi-Cal or the California Children's Services (CCS) Program may cover the cost of any necessary diagnostic services. The Newborn Screening Program (NBSP) will be responsible for costs services associated with the initial diagnostic testing done at a CCS Metabolic Center that are not covered by the patient's health insurance carrier, Medi-Cal, or the CCS Program.
- The NBSP will not pay for services provided outside CCS Metabolic Centers.
- Treatment services are not covered by NBSP. However, the patient's health insurance, Medi-Cal or the CCS Program may pay for these services.

Role of Prenatal Care Providers/Birth Attendants: Informed Consent

Prenatal care providers are required by law to distribute a copy of the informational material, entitled *Important Information for Parents About the Newborn Screening Test (IIP)*, which describes the mandatory newborn screening program.[2] During the research project written documentation of informed consent will be required for the voluntary supplemental testing. To help facilitate this process, the information about the mandatory program and the voluntary supplemental testing has been combined into one booklet. The informed consent form will be signed in the hospital prior to blood specimen collection from the newborn.

Prenatal care providers will need to make sure that all women who are due to deliver during the pilot period (starting on or shortly after January 7, 2002) receive a copy of the revised Newborn Screening Program booklet and have their questions answered regarding the MS/MS research project. ***The consent form should be signed in the hospital, not the physician's office.*** Birth attendants in the hospital will be responsible for ensuring that women who do not obtain prenatal

[2] California Code of Regulations, Title 17, Subchapter 9 Heritable Diseases, Sections 6500-6508

care receive information on both the mandatory program and the voluntary supplemental newborn screening programs prior to specimen collection.

Role of Hospitals/Birthing Centers

Hospitals and birthing center staff, using the form included in the Newborn Screening program booklet, will obtain written verification of informed consent. Staff will indicate whether the newborn is to be enrolled in the supplemental study by affixing color-coded stickers (indicating "YES" or "NO") to the filter paper and demographic sheet of the Test Request Form***. The supplemental testing will only be done on initial adequate specimens with a "YES" sticker on the filter paper.***

Role of Metabolic Centers

Metabolic physician specialists will be available to answer questions about the program, the MS/MS technology and the disorders being tested. The metabolic centers will make the arrangements for confirmatory testing and develop the diagnostic and treatment plan, which will be shared with the newborns primary care provider and the NBSP. Based upon experience of the pilot project and input from metabolic specialists, follow-up guidelines for these disorders will be developed.

Additional Information

The *Important Information for Parents About the Newborn Screening Test (IIP)* booklet, explains both the current mandatory screening (in the first few pages of the booklet on the white pages) and the supplemental research testing (in the purple pages in the center of the booklet). The booklet is in both English and Spanish (booklets translated to Chinese, Vietnamese, Cambodian, and Korean are also available). Providers or patients who have questions can call the MS/MS Follow-up Coordinator at (866) 954-BABY (954-2229) toll free for additional information. Questions may also be e-mailed to msms@dhs.ca.gov.